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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,528	10/13/2000	David M. Stern	0575/62096/JPW/JML	8939

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EXAMINER

CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/687,528

Applicant(s)

STERN ET AL.

Examiner

Shin-Lin Chen

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 March 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-5 and 11-14 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 3-5 and 11-14 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Art Unit: 1632

DETAILED ACTION

Applicants' response filed 3-2-05 has been entered. Claims 3-5 and 11-14 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 3-5 and 11-14 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reduction of smooth muscle proliferation and migration in carotid artery by treating Fatty Zucker rat with murine soluble RAGE (sRAGE) via intraperitoneal injection, does not reasonably provide enablement for a method for preventing exaggerated restenosis in a diabetic subject by administering to said subject any sRAGE polypeptide other than murine sRAGE in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons of record. Applicant's arguments filed 3-2-05 have been fully considered but they are not persuasive.

Applicants argue that no undue experimentation is required to practice the claimed invention and the specification provides a representative number of sRAGE to enable the pending claims on pages 13-19 of the specification (response, p. 3). This is not found persuasive because of the reasons of record. The specification only provides the nucleotide and amino acid sequences of human, bovine, and mouse RAGE. The specification only provides the biological

Art Unit: 1632

function of mouse soluble RAGE but fails to provide adequate guidance and evidence whether the soluble RAGE of human or bovine origin would have the same biological function as that of the mouse sRAGE. The claims encompass using numerous sRAGEs, which have different amino acid sequences, derived from various organisms, such as humans, cows, horses, rats, mice, sheep, other mammals, fishes, insects etc., to prevent exaggerated restenosis in a diabetic subject *in vivo*. The statement on page 31 lines 8-9 of the specification only identifies that the sRAGE is the extracellular ligand-binding domain of the receptor, however, no detailed information for the structural feature of sRAGE that contributes to prevent exaggerated restenosis has been provided. Since the amino acid sequences of sRAGE derived from different organisms would vary and one skilled in the art at the time of the invention would not know whether they would have the same biological function as the mouse sRAGE to reduce the smooth muscle proliferation and migration in carotid artery. It was known in the art that same stretch of an amino acid sequence can contribute to different biological functions in different proteins. Further, the biological function of a polypeptide was unpredictable from mere amino acid sequence at the time of the invention, therefore, it would require one skilled in the art undue experimentation to practice over the full scope of the invention claimed.

3. Claim 4 remains rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reduction of smooth muscle proliferation and migration in carotid artery by treating Fatty Zucker rat with murine soluble RAGE (sRAGE) via intraperitoneal injection, does not reasonably provide enablement for a method for preventing exaggerated restenosis in a diabetic **human** subject by administering to said subject any sRAGE polypeptide *in vivo*. The

Art Unit: 1632

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons of record. Applicant's arguments filed 3-2-05 have been fully considered but they are not persuasive.

Applicants cite Dr. Ann Marie Schmidt's declaration and argue that the Muller, Reilly and Lafont references cited by examiner do not discuss the fatty Zucker rat model used in the present invention. Applicants cite reference Park et al., and argue that the fatty Zucker rat is a well-established model of type II diabetes, and the arteries of fatty Zucker rats are diseased and its response to carotid balloon injury parallels the results observed in diabetic human subjects. Applicants further comment on "Study Limitations" made by Park (response, p. 4-6). This is not found persuasive because of the reasons of record. As reported by Miller, significant interspecies and intraspecies differences were found to exist among the various animal models, particularly with respect to the extent and composition of neointimal thickening, drug and lipid metabolism, and the activity of coagulation and fibrinolytic systems. The amount of elastin in the media of coronary arteries of larger animals, such as dogs, pigs and baboons, are very similar to that of the human coronary artery but greater than that in small species, such as rodents and fowls, and thickness of the arterial intima varies among species. "Rat arteries differ morphologically from human arteries in that they have no vasa vasorum, have a very much thinner subintimal layer and have a relatively small elastin content in the media (e.g. p. 421, left column, lines 4-7). The concerns stated by Miller are reflected in the statement by Park reference cited by applicants. Park states "This study has several limitations. The relevance of restenotic animal models to human restenosis is unknown, and no single model has yet been

Art Unit: 1632

shown to reliably predict restenosis in humans” (p. 819, left column under “Study Limitations”). Although fatty Zucker rat model has disease arteries and is a well-established model for type II diabetes, however, whether the data of fatty Zucker rat regarding the use of a drug or sRAGE to prevent exaggerated restenosis is predictive of the therapeutic effect of the drug or sRAGE in a diabetic human subject is still unknown. One cannot extrapolate success in preventing exaggerated restenosis in fatty Zucker rat into success in a diabetic human subject. Therefore, although animal studies are likely to provide important insights into the pathophysiology of vascular injury, Park states “no single model has yet been shown to reliably predict restenosis in humans”. Thus, claim 4 remains rejected under 35 U.S.C. 112, first paragraph.

Conclusion

No claim is allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

Art Unit: 1632

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER